REMARKS

Claims 1-24 were previously cancelled. Claims 26, 29-31, 33 and 36 stand withdrawn from consideration as drawn to a non-elected invention. Claims 25, 27, 28, 32, 34 and 35 are presently pending and under examination. Claim 25 has been amended to recite only the Substance P analogs rather than Substance P itself as well as the analogs thereof. No new matter is added by the amendment to claim 25 and entry thereof is respectfully requested.

Regarding 35 U.S.C. § 112, Second Paragraph

Claims 25, 32 and 34 stand rejected under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite because of the term "analog." Applicants respectfully traverse the rejection. According to the Office Action, core structures of both Substance P (claim 25) and a toxin fragment (claims 32 and 34) necessary for their functional characteristics are not taught and, therefore, the skilled person cannot ascertain what is entailed in the term "analog."

A seminal case on the construction of the second paragraph of § 112 is *In re Borkowski*, 422 F.2d 904, 164 U.S.P.Q. 642 (C.C.P.A. 1970), where the CCPA observed:

> The first sentence of the second paragraph of § 112 is essentially a requirement for precision and definiteness of claim language. If the scope of subject matter embraced by a claim is clear, and if the applicant has not otherwise indicated that he intends that claim to be of a different scope, then the claim does particularly point out and distinctly claim the subject matter which the applicant regards as his invention.

Id. at 909, 164 U.S.P.Q. at 645-46 (footnote omitted).

The Federal Circuit has since had the opportunity to decide a number of § 112, second paragraph issues. It is clear from these decisions that definiteness of claim language must be analyzed, not in a vacuum, but in light of (1) the content of the particular application disclosure, (2) the teachings of the prior art, and (3) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made. *See, e.g., In re Marosi*, 710 F.2d 799, 218 U.S.P.Q. 289 (Fed. Cir. 1983); *Rosemount, Inc. v. Beckman Instruments, Inc.*, 727 F.2d 1540, 221 U.S.P.Q. 1 (Fed. Cir. 1984); *W.L. Gore &*

Assocs., Inc. v. Garlock, Inc., 721 F.2d 1540, 220 U.S.P.Q. 303 (Fed. Cir. 1983); and *Atmel Corp. v. Information Storage Devices, Inc.*, 198 F.3d 1374, 53 U.S.P.Q.2d 1225 (Fed. Cir. 1999) (district court failed to consider the knowledge of one skilled in the art when interpreting the patent disclosure).

> The primary purpose of the definiteness requirement is to ensure that the claims are written in such a way that they give notice to the public of the extent of the legal protection afforded by the patent, so that interested members of the public, e.g., competitors of the patent owner, can determine whether or not they infringe. That determination requires a construction of the claims according to the familiar canons of claim construction.

All Dental Prodx, LLC v. Advantage Dental Prods., 309 F.3d 774, 779-80, 64 USPQ2d 1945, 1949 (Fed. Cir. 2002) (citations omitted).

Substance P Analogs

With regard to claim 25 and the Substance P analog, the scope is very clear and definite given that the two analogs encompassed by the claim are recited in the claim. In particular, claim 25 is directed to a conjugate comprising of a Substance P analog and a polypeptide that inhibits protein synthesis, and recites that "the analog **is selected from** CYGGGGGGRPKPQQFF SarLMet(O2)-amide (SEQ ID NO:1) and CYGGGGGGRPKPQQFFGLM-amide (SEQ ID NO:2)." Therefore, the skilled person can ascertain with clarity that the two recited analogs of Substance P are embraced by the term "analog."

Pseudomonas aeruginosa exotoxin A Analogs

Contrary to the Office's assertion, neither claim 32 nor its base claim (Claim 1) recites a toxin analog. With regard to claim 34, it is respectfully submitted that the skilled person, at the time of filing, would have understood with clarity the functional characteristics of a pseudomonas aeruginosa exotoxin A analog and the core structure responsible for the catalytic action. The Office's assertion that claim 34 encompasses broadly the inhibition synthesis of any protein, including the toxin itself is respectfully submitted to be a tortured and improper interpretation of the claim in a complete vacuum that is completely divorced from the intrinsic record, in particular the specification.

Applicants submit herewith as Appendix A to the Response a 1996 publication by Li et al., Proc. Natl. Acad. Sci USA, 93:6902-6906 (1996), and direct the Examiner's attention to the introductory paragraphs at page 6902. It is clear based upon the introductory paragraphs, replete with citations to art-known publications, that Pseudomonas exotoxin A, along with diphtheria toxin, E. coli heat labile enterotoxin and pertussis toxin, belongs to a group of bacterial toxins that target proteins in eukaryotic cells. See first paragraph following abstract, at p. 6902. Thus, the skilled person would have known, for example, that the toxin does not inhibit its own synthesis. Furthermore, this publication, which forms part of the state of the art at the time of filing, shows that the core structures responsible for the toxin's functional activities were known to those skilled in the art. See, in particular, p. 6902, paragraph bridging left and right column. In addition to describing the core structures responsible for the toxin's action, analogs are described: "The function of domain Ib (residues 365-399) is unknown and can be entirely deleted without loss of toxin activity." p. 6902, right column, first full sentence. Applicants further submit as Appendix B a publication by Siegall et al., J. Biol. Chem. 24:14256-14261(1089) entitled "Functional Analysis of Domains II, Ib, and III of Pseudomonas Exotoxin," which reports the preparation and testing of mutant proteins for their ADP-ribosylation, EGF receptor-binding, and cell- killing activities. It is respectfully submitted that in view of (1) the content of the particular application disclosure, (2) the teachings of the prior art, and (3) the claim interpretation that would be given by one possessing the ordinary level of skill in the pertinent art at the time the invention was made, the term "analog" is clear and definite. Accordingly, Applicants request removal of the rejection of claims 25, 32 and 34 under 35 U.S.C. § 112, second paragraph, for allegedly being indefinite.

Regarding 35 U.S.C. §102(a)

The rejection of claims 25, 27, 28, 32, 34 and 35 under 35 U.S.C. §102(a) as anticipated by Leeman et al., WO 97/13410, is respectfully traversed. Applicants respectfully submit that this rejection has been rendered moot by the amendment to claim 25 , which now recites a conjugate including a Substance P analog and a polypeptide that inhibits protein synthesis, wherein the analog is selected from CYGGGGGGRPKPQQFF SarLMet(O2)-amide (SEQ ID NO:1) and CYGGGGGGRPKPQQFFGLM-amide (SEQ ID NO:2). Removal of the rejection of

claims 25, 27, 28, 32, 34 and 35 under 35 U.S.C. §102(a) as anticipated by Leeman et al., WO 97/13410, is respectfully requested.

Regarding Obviousness-type Double Patenting

The rejection of claims 25, 27, 28, 32, 34 and 35 under the judicially created doctrine of obviousness-type double patenting as allegedly unpatentable over claims 1-9 of U.S. Patent No. 6,063,758, is respectfully traversed. Applicants respectfully request that this rejection be held in abeyance until there is an indication of allowable subject matter.

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Respectfully submitted,

McDERMOTT WILL & EMERY LLP

Astrid R. Spain
Registration No. 47,956

4370 La Jolla Village Drive, Suite 700
San Diego, CA 92122
Phone: 858.535.9001 ARS:cjh
Facsimile: 858.597.1585

Date: March 6, 2007

SDO 58726-1.066785.0017

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